WHAT IS CLAIMED IS:

1. A substantially purified single chain or multi-chain polypeptide, selected from:

a) a polypeptide, comprising a protease domain of a serine protease 16 (CVSP16) or a functionally active portion thereof or a domain thereof, wherein: if the polypeptide includes residues that correspond to Gln_{660} and Met_{661}, it does not include at least 5 contiguous amino acids from SEQ ID No. 21 inserted between residues that correspond to Gln_{660} and M_{661} of SEQ ID No. 21; or

b) a substantially purified single chain or multi-chain polypeptide, comprising at least two protease domains of a serine protease 16 (CVSP16), wherein the polypeptide comprises at least 5 contiguous amino acids corresponding to residues 508-544 of SEQ ID No. 6. or comprises the contiguous sequence Asn Asp Ser or Trp Asn Asp or Ser Cys Trp Asn Asp Ser or Cys Trp Asn Asp Ser or Gln Thr His or Leu Gln Thr His in the second protease domain.

2. The polypeptide of claim 1, wherein one protease domain comprises amino acids 323-550 or 326-550 of SEQ ID No. 6. or has at least about 60%, 70%, 80%, 90% or 95% sequence identity to amino acids 326-550 of SEQ ID No. 6.

3. The polypeptide of claim 1, wherein one protease domain comprises amino acids 46-286 of SEQ ID No. 6 or as has at least about 60%, 70%, 80%, 90% or 95% sequence identity to amino acids 47-286 of SEQ ID No. 6.

4. A polypeptide of claim 1 that contains two or three chains.

5. A substantially purified single chain or multi-chain polypeptide of claim 1, comprising a protease domain of a serine protease 16 (CVSP16) or a catalytically active portion thereof or a domain thereof, wherein the polypeptide does not include at least 5 contiguous amino acids from SEQ ID No. 21; and the polypeptide contains one, two or three chains.

6. A polypeptide of claim 1 that comprises one protease domain.

7. A polypeptide of claim 1 that comprises two protease domains.

8. A polypeptide of claim 1 or claim 5, wherein a protease domain comprises amino acids 46-286 or 326-550 of SEQ ID No. 6 or amino acids that share at least about 60%, 70%, 80%, 90% or 95% homology to amino acids 46-286 or 326-550 of SEQ ID No. 6.

9. A polypeptide of claim 1 or claim 5, wherein the contiguous sequence is not present in the polypeptide at any locus.

10 . A polypeptide of claim 1 or claim 5, wherein the polypeptide comprises the contiguous sequence Gly His Gln Met Thr Ser (SEQ ID No. 6, amino acids 658-663).

11. A polypeptide of claim 7, that comprises amino acids 46-286 and 326-550 of SEQ ID No. 6 or amino acids that share at least about 60%, 70%, 80%, 90% or 95% sequence identity to each of amino acids 46-286 and and amino acids 326-550 of SEQ ID No. 6.

12. A polypeptide of claim 1 or claim 5, wherein the CVSP16 portion of the polyeptide consists essentially of amino acids 46-286 of SEQ ID No. 6.

13. A polypeptide of claim 1 or claim 5, wherein the CVSP16 portion consists essentially of amino acids 323-550 or 326-550 of SEQ ID No. 6.

14. A polypeptide of claim 12, wherein the CVSP16 portion of the polyeptide has at least about 60%, 70%, 80%, 90% or 95% sequence identity to amino acids 46-286 of SEQ ID No. 6.

15. A polypeptide of claim 13, wherein the CVSP16 portion of the polyeptide has at least about about 60%, 70%, 80%, 90% or 95% sequence identity to amino acids 46-286 of SEQ ID No. 6.

16. A polypeptide of claim 5, wherein the CVSP16 portion of the polypeptide consists essentially of amino acids 46-550 of SEQ ID No. 6.

17. The polypeptide of claim 5, wherein:

the CVSP16 portion of the polypeptide consists essentially of a protease domain of a CVSP16 or a catalytically active portion thereof.

18. A polypeptide of claim 1, comprising the sequence of amino acids set forth in SEQ ID No. 6 or set forth as amino acids 24-752 in SEQ ID No. 6.

19. A polypeptide of claim 5, consisting essentially of the sequence of amino acids set forth in SEQ ID No. 6 or consisting essentially of amino acids 24-752 or SEQ ID No. 6.

20. A polypeptide of claim 5, wherein the CVSP16 is a human protein.

21. A polypeptide of claim 1 that has catalytic activity.

22. A polypeptide of claim 5, wherein the level of expression and/or activity of the CVSP16 in tumor cells differs from its level of expression and/or activity in non-tumor cells.

23. A polypeptide of claim 5, wherein the CVSP16 polypeptide is detectable in a body fluid at a level that differs from its level in body fluids in a subject not having a tumor.

24. A polypeptide of claim 1 or claim 5 that is a single chain.

25. A polypeptide of claim 5 that is a two or three chain polypeptide.

26. A polypeptide of claim 1, wherein:

the CVSP16 is present in a tumor; and

a substrate or cofactor for the CVSP16 is expressed at levels that differ from its level of expression in a non-tumor cell in the same type of tissue.

27. A polypeptide of claim 1 that has at least about 60%, 80%, 90% or 95% sequence identity with a polypeptide that comprises the sequence of amino acids set forth as SEQ ID No. 6 or a catalytically active portion thereof.

28. A polypeptide of claim 1 that comprises a protease domain encoded by a nucleic acid molecule selected from the group consisting of:

a) a nucleic acid molecule that hybridizes under conditions of high stringency along at least 70% of its full length to a nucleic acid molecule comprising a sequence of nucleotides set forth in SEQ ID No. 5 that encodes amino acids 46 to 285 or 326 to 550 of SEQ ID No. 6;

b) a nucleic acid molecule molecule, comprising the sequence of nucleotides set forth in SEQ ID No. 5 that encodes resides 24-752; and

c) a nucleic acid molecule that comprises degenerate codons of a) or b).

29. A polypeptide of claim 5 that is selected from the group consisting of:

a polypeptide encoded by the sequence of nucleotides set forth in SEQ ID No. 5 or a catalytically active portion or ligand or substrate binding portion of the polypeptide;

a polypeptide encoded by a sequence of nucleotides that hybridizes under conditions of high stringency along 70% of its full length to the sequence of nucleotides set forth in SEQ ID No. 5 or to a sequence of nucleotides comprising degenerate codons thereof;

a polypeptide that comprises a sequence of amino acids having at least about 85%, 86%, 88%, 90%, 93% or 95% sequence identity with the sequence of amino acids set forth in SEQ ID No. 6; and

a polypeptide encoded by a splice variant of the sequence of nucleotides set forth in SEQ ID No. 5.

30. A polypeptide that is a mutein of the polypeptide of claim 1 or claim 5, wherein:

up to about 50% of the amino acids are replaced with another amino acid; and

the resulting polypeptide is a single chain two-chain or three-chain polypeptide that has catalytic activity of at least 1% of the unmutated polypeptide.

31. A polypeptide of claim 30, wherein up to about 25% of the amino acids are replaced with another amino acid.

32. A polypeptide of claim 30, wherein up to about 10% of the amino acids are replaced with another amino acid.

33. A polypeptide of claim 30, wherein the resulting polypeptide is a single chain or two-chain or three-chain polypeptide and has catalytic activity of at least 10% of the unmutated polypeptide.

34. A polypeptide of claim 32, wherein the resulting polypeptide is a single chain or two-chain or three-chain polypeptide and has catalytic activity of at least 10% of the unmutated polypeptide.

35. A polypeptide of claim 30, wherein up to about 95% of the amino acids are conserved or are replaced by conservative amino acid substitutions.

36. A polypeptide of claim 1 or claim 5, wherein an unpaired Cysteine in a protease domain is replaced with another amino acid.

37. The polypeptide of claim 36, wherein the replacing amino acid is a serine.

38. A polypeptide of claim 36, wherein the unpaired Cys in a protease domain is amino acid C_{159} and/or C_{430}.

39. A nucleic acid molecule, comprising a sequence of nucleotides that encodes a polypeptide of claim 1 or claim 5.

40. A plasmid or vector comprising the nucleic acid molecule of claim 39.

41. A vector of claim 40 that is an expression vector.

42. A vector of claim 41 that includes a sequence of nucleotides that directs secretion of any protein encoded by a sequence of nucleotides operatively linked thereto.

43. A vector of claim 41 that is a *Pichia* vector, a baculovirus vector, an mammalian cell vector or an *E. coli* vector.

44. A cell, comprising a plasmid or vector of claim 40.

45. The cell of claim 44 that is a prokaryotic cell.

46. The cells of claim 44 that is a eukaryotic cell.

47. The cell of claim 44 that is selected from among a bacterial cell, a yeast cell, a yeast cell, a plant cell, an insect cell and an animal cell.

48. The cell of claim 47 that is a mammalian cell.

49. A method for producing a polypeptide that contains a protease domain of a CVSP16, comprising:

culturing a cell of claim 44 under conditions whereby the encoded protein is expressed by the cell; and

recovering the expressed protein.

50. The method of claim 49, wherein the cell is a *Pichia* cell and the protein is optionally secreted into the culture medium or the cell is a mammalian cell.

51. The method of claim 49, wherein the polypeptide is secreted into the culture medium.

52. The method of claim 49, wherein the polypeptide is expressed in the cytoplasm of the host cell.

53. The method of claim 49, wherein the polypeptide is expressed in inclusion bodies, and the method further comprises

isolating the polypeptide from the inclusion bodies under conditions, whereby the polypeptide refolds into a proteolytically active form.

54. An antisense nucleic acid molecule that:

comprises at least 14 and less than about 150 contiguous nucleotides or modified nucleotides that are complementary to a contiguous sequence of nucleotides of a CVSP16 of claim 5;

comprises at least 16 and less than about 150 contiguous nucleotides or modified nucleotides that are complementary to a contiguous sequence of nucleotides of a CVSP16 of claim 5;

comprises at least 30 and less than about 150 contiguous nucleotides or modified nucleotides that are complementary to a contiguous sequence of nucleotides of a CVSP16 of claim 5,

wherein the contiguous nucleotides span nucleotides corresponding to nucleotides 1978-1983 of SEQ ID No. 5.

55. A double-stranded RNA (dsRNA) molecule that comprises at least about 21 contiguous nucleotides or modified nucleotides that are complementary to all or a portion of a contiguous sequence of nucleotides that encodes the sequence of amino set forth as SEQ ID No. 6.

56. The dsRNA of claim 55, wherein the contiguous nucleotides span nucleotides corresponding to nucleotides 1978-1983 of SEQ ID No. 5.

57. An antibody that binds to a polypeptide of claim 5 with at least 10-fold greater affinity than to a polypeptide that includes the at least 5 contiguous amino acids set forth in SEQ ID No. 21.

58. An antibody that binds to a polypeptide of claim 5 with at least 2-fold greater affinity than to a polypeptide that includes the at least 5 contiguous amino acids set forth in SEQ ID No. 21.

59. The antibody of claim 58, wherein the contiguous sequence is inserted between amino acids corresponding to Q660 and M661 of a CVSP16 polypeptide that comprises amino acids 24-752 of SEQ ID No. 6.

60. An antibody of claim 57 that binds with at least 100-fold greater affinity.

61. An antibody of claim 58 that inhibits an catalytic activity of the polypeptide.

62. An antibody of claim 58 that inhibits an a ligand or substrate binding activity of the polypeptide.

63. An antibody that specifically binds to a single-chain form of a protease domain 1 (PD1) of a CVSP16 polypeptide or to a single-chain form of a protease domain 2 (PD2) of a CVSP16 polypeptide.

64. An antibody of the specifically that binds to a single-chain form of a CVSP16 polypeptide of claim 5.

65. A conjugate, comprising:

a) a CVSP16 polypeptide; and

b) a targeting agent linked to the protein directly or via a linker.

66. A combination, comprising:

a) a modulator of the catalytic activity or substate or ligand binding activity of a CVSP16 polypeptide; and

b) another treatment agent or agent selected from anti-tumor and anti-angiogenic treatments or agents.

67. The combination of claim 66, wherein the modulator is an inhibitor.

68. The combination of claim 67, wherein the inhibited activity is catalytic activity.

69. The combination of claim 68, wherein the modulator inhibitor and the anti-tumor and/or anti-angiogenic agent are formulated in a single pharmaceutical composition or each is formulated in separate pharmaceutical compositions.

70. The combination of claim 69, wherein the inhibitor is selected from antibodies and antisense oligonucleotides.

71. A solid support comprising two or more CVSP16 polypeptides of claim 5 linked thereto either directly or via a linker.

72. The support of claim 71, wherein the polypeptides comprise an array.

73. The support of claim 71, further comprising a plurality of different serine protease domains linked to the support directly or via a linker.

74. A method for identifying compounds that modulate the protease activity of a CVSP16 polypeptide, comprising:

contacting a polypeptide of claim 5 with a substrate proteolytically cleaved by the CVSP16 polypeptide, and, either simultaneously, before or after, adding a test compound or plurality thereof;

measuring the amount of substrate cleaved in the presence of the test compound; and

selecting compounds that change the amount cleaved compared to a control, whereby compounds that modulate an activity of the CVSP16 are identified.

75. The method of claim 74, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

76. The method of claim 74, wherein a plurality of the test substances are screened simultaneously.

77. The method of claim 74, wherein the change in the amount of substrate cleaved is assessed by comparing the amount cleaved in the presence of the test compound with the amount cleaved in the absence of the test compound.

78. The method of claim 74, wherein the polypeptides comprise an array.

79. The method of claim 74, wherein the polypeptides comprise a plurality of different serine proteases.

80. A method of identifying a compound that specifically binds to a form of a CVSP16, comprising:

contacting a CVSP16 polypeptide of claim 5, or a functionally active portion thereof, with a test compound or plurality thereof under conditions conducive to binding thereof, and either:

a) identifying test compounds that specifically bind to a form, or to a functionally active portion thereof; or

b) identifying test compounds that inhibit binding of a compound known to bind to a form of the polypeptide or to a functionally active portion thereof, wherein:

the known compound is contacted with the polypeptide either before, simultaneously with, or after the test compound;

a functionally active portion is a proteolytically active portion and/or a substrate or ligand binding portion; and

a form is one or more of a single chain form, a two-chain form, a three chain form and/or a four chain form and the form is activated or is a zymogen or includes one or more activated domains.

81. The method of claim 80, wherein the polypeptide is linked either directly, or indirectly, via a linker, to a solid support.

82. The method of claim 80, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

83. The method of claim 80, wherein a plurality of the test substances are screened simultaneously.

84. The method of claim 83, wherein a plurality of the polypeptides are linked to a solid support.

85. A method for identifying activators of a zymogen form of a CVSP16 or functionally active thereof, comprising:

contacting a zymogen form of a CVSP16 polypeptide of claim 5, or a functionally active portion thereof, with a substrate of the activated form of the polypeptide;

adding a test compound, wherein the test compound is added before, after, or simultaneously with, the addition of the substrate; and

detecting cleavage of the substrate, thereby identifying compounds that activate the zymogen, wherein:

a functionally active portion is a proteolytically active portion and/or a substrate or ligand binding portion; and

a zymogen is one or more of a single chain form, a two-chain form or a three chain form that includes at least one domain that is not activated.

86. The method of claim 85, wherein the substrate is a chromogenic or fluorogenic substrate.

87. The method of claim 85, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

88. A method for treating or preventing a neoplastic disease in a mammal, comprising administering to a mammal an effective amount of a modulator of a polypeptide of claim 5.

89. The method of claim 88, wherein the modulator is an inhibitor.

90. The method of claim 88, wherein the modulator is an antibody that specifically binds to the polypeptide, or a fragment or derivative of the antibody containing a binding domain thereof, wherein the antibody is a polyclonal antibody or a monoclonal antibody.

91. A method of inhibiting tumor initiation, growth, progression, or treatment of a malignant or pre-malignant condition, comprising administering an agent that modulates activation cleavage of the zymogen form of a CVSP16 polypeptide of claim 5 or a potentially functionally active portion thereof, or inhibits an activity of the activated form of CVSP16, or a proteolytically active portion thereof, wherein a functionally active portion is a proteolytically active portion and/or a substrate or ligand binding portion.

92. The method claim 91, wherein the agent inhibits cleavage.

93. The method of claim 91, wherein the condition is a tumor or cancer of the uterus, breast, colon, lung, kidney, rectum, prostate, cervix, testes, stomach, esophagus, ovary, or small intestine, or is a leukemia or a lymphoma.

94. The method of claim 91, wherein the agent is an antisense oligonucleotide, double-stranded RNA (dsrna) or an antibody.

95. The method of claim 91, further comprising administering another treatment or agent selected from anti-tumor and anti-angiogenic treatments or agents.

96. A method of identifying a compound that binds to one or more forms of a CVSP16 polypeptide of claim 5, and/or to a functionally active portion thereof comprising:

contacting a test compound with two or more forms of a CVSP16 polypeptide of claim 5;

and determining to which form or forms the compound binds; and

if it binds to a form of a CVSP16 polypeptide, further

determining whether the compound has at least one of the following properties:

(i) inhibits activation cleavage of a zymogen form of polypeptide;

(ii) inhibits activity of a form; and

(iii) inhibits dimerization of the polypeptide, wherein:

a functionally active portion is a catalytically active portion and/or a substrate or ligand binding portion; and

a form is one or more of a single chain form, a two-chain form, a three chain form and/or a four chain form and the form is activated or is a zymogen or includes one or more activated domains.

97. A method of detecting neoplastic disease, comprising:

detecting a polypeptide that comprises a polypeptide of claim 5 in a biological sample, wherein the amount, form, and/or activity detected differs from the amount, form, and/or activity of the polypeptide detected from a subject without neoplastic disease.

98. The method of claim 97, wherein the biological sample is selected from the group consisting of blood, urine, saliva, tears, synovial

fluid, sweat, interstitial fluid, sperm, cerebrospinal fluid, ascites fluid, and/or tumor tissue biopsy and circulating tumor cells.

99. The method of claim 96, wherein the biological sample is selected from the group consisting of blood, urine, saliva, tears, synovial fluid, sweat, interstitial fluid, cerebrospinal fluid, semen, ascites fluid, tumor tissue biopsy and circulating tumor cells.

100. The method of claim 97, wherein the one or more forms of the CVSP16 polypeptide consist(s) essentially of a protease domain.

101. A method of diagnosing the presence of a pre-malignant lesion, malignancy, or other pathologic condition in a subject, comprising:

obtaining a biological sample from the subject;

exposing it to an agent that binds to one or more forms of a CVSP16 polypeptide or inhibits or potentiates an activity of the polypeptide; and

detecting binding and/or a change in the activity,

wherein:

the pathological condition is characterized by the presence, excess or absence of a three-chain, two-chain and/or single-chain form; and

detection of binding and/or a change in the activity is indicative of the pathological condition in the subject.

102. The method of claim 101, wherein an activity is inhibited.

103. The method of claim 101, wherein the agent is an antibody that specifically binds to a CVSP16 polypeptide.

104. The method of claim 101, wherein the sample is bodily fluid selected from blood, urine, sweat, saliva, cerebrospinal fluid or synovial fluid.

105. A method of monitoring tumor progression and/or therapeutic efficacy, comprising detecting and/or quantifying the level, form, and/or activity of a CVSP16 polypeptide in a bodily tissue or fluid sample.

106. The method of claim 105, wherein the tumor is a tumor of the uterus, breast, colon, lung, kidney, rectum, prostate, cervix, testes, stomach, esophagus, ovary, or small intestine, or is a leukemia or a lymphoma

107. The method of claim 105, wherein the bodily fluid is blood, urine, sweat, saliva, cerebrospinal fluid or synovial fluid.

108. A method of inhibiting tumor invasion or metastasis or treating a malignant or pre-malignant condition, comprising administering an agent that inhibits activation of the zymogen form of CVSP16 or an activity of an activated form.

109. The method of claim 108, wherein the condition is a condition of the uterus, breast, colon, lung, kidney, rectum, prostate, cervix, testes, stomach, esophagus, ovary, or small intestine, or is a leukemia or a lymphoma.

110. The method of claim 108, further comprising administering another treatment or agent selected from anti-tumor and anti-angiogenic treatments or agents.

111. The method of claim 108, wherein the agent is an antisense oligonucleotide or an antibody.

112. A signal sequence, consisting essentially of amino acids 1-23 of SEQ ID No. 6.

113. A pro-polypeptide, comprising the signal sequence of claim 107, wherein the signal sequence is heterologous to a polypeptide operatively linked thereto.

114. A polypeptide, comprising a portion of a CVSP16 polypeptide, wherein the portion consists essentially of amino acids 1-23 of SEQ ID No. 6.

115. A computational method for screening compounds, comprising:

assessing the interaction of a test compound with a computer-simulated polypeptide that has the sequence of amino acids of a polypeptide of any of claims 1, 4 and 6; and

identifying test compounds that interact with the polypeptide, wherein assessment is effected *in silico*.

116. A recombinant non-human animal, wherein an endogenous gene that encodes a polypeptide of claim 4 has been deleted or inactivated by homologous recombination or insertional mutagenesis of the animal or an ancestor thereof.

117. A transgenic non-human, comprising heterologous nucleic acid that enodes a polypeptide of claim 4.

118. The conjugate of claim 65, wherein the targeting agent permits

i) affinity isolation or purification of the conjugate;

ii) attachment of the conjugate to a surface;

iii) detection of the conjugate; or

iv) targeted delivery to a selected tissue or cell.